

JUL 20 2009

PATENT APPLN. NO. 10/524,892
RESPONSE UNDER 37 C.F.R. §1.116

PATENT
FINAL

IN THE CLAIMS:

1. (currently amended) A modified substrate comprising a hydrophilic polymer and a precursor substrate, the hydrophilic polymer being covalently bonded to a surface of the precursor substrate to the extent that a ratio of the hydrophilic polymer of the modified substrate that is not covalently bonded to the surface of the precursor substrate to the total of the hydrophilic polymer of the modified substrate is 15 weight percent or less and a number of adhered human blood platelets is $10/4.3 \times 10^3 \mu\text{m}^2$ or less when the modified substrate is brought into contact with human blood which contains heparin with a concentration of 50 U/mL at 37°C for one hour.

2. (previously presented) The modified substrate according to claim 1, wherein the modified substrate is obtainable by irradiating with radiation while the precursor substrate is brought into contact with an aqueous solution of the hydrophilic polymer.

3. (original) The modified substrate according to claim 2, wherein, in the aqueous solution of the hydrophilic polymer, the maximum increasing value of ultraviolet absorption value in the

PATENT APPLN. NO. 10/524,892
RESPONSE UNDER 37 C.F.R. §1.116

PATENT
FINAL

wavelength range of 260 to 300 nm, the increase being caused by irradiating with radiation, is 1 or less.

4. (previously presented) The modified substrate according to claim 2, wherein the modified substrate is obtainable by irradiating with radiation while the precursor substrate is brought into contact with an aqueous solution containing the hydrophilic polymer and an antioxidant.

5. (original) The modified substrate according to claim 4, wherein, in the aqueous solution of the hydrophilic polymer, the maximum increasing value of ultraviolet absorption value in the wavelength range of 260 to 300 nm, the increase being caused after irradiating with radiation, is 1 or less.

6. (previously presented) The modified substrate according to claim 1, wherein a surface hydrophilic polymer ratio is at least 20 weight percent.

7. (previously presented) The modified substrate according to claim 1, wherein the modified substrate comprises a plurality of hydrophilic polymers.

PATENT APPLN. NO. 10/524,892
RESPONSE UNDER 37 C.F.R. §1.116

PATENT
FINAL

8. (previously presented) The modified substrate according to claim 7, wherein the modified substrate comprises a cationic hydrophilic polymer and a nonionic hydrophilic polymer.

9. (previously presented) The modified substrate according to claim 7, wherein the modified substrate comprises an anionic hydrophilic polymer and a nonionic hydrophilic polymer.

10. (currently amended) The modified substrate according to claim 1, wherein the amount of the hydrophilic polymer that is not covalently bonded to the substrate is 0.5 mg/m² or less.

11. (original) The modified substrate according to claim 1, wherein the hydrophilic polymer is a polyalkylene glycol or polyvinylpyrrolidone.

12. (original) The modified substrate according to claim 1, wherein the hydrophilic polymer is a polymer derived from the living body.

PATENT APPLN. NO. 10/524,892
RESPONSE UNDER 37 C.F.R. §1.116

PATENT
FINAL

13. (previously presented) The modified substrate according to claim 1, wherein an adsorptivity to interleukin-6 is at least 0.1 ng/cm².

14. (previously presented) The modified substrate according to claim 13, wherein the hydrophilic polymer is a polyalkylene glycol and the bonding density of the polyalkylene glycol is 150 to 3,000 mg/m².

15. (previously presented) The modified substrate according to claim 13, wherein the precursor substrate is a material comprising a hydrophobic polymer.

16. (currently amended) The A modified substrate according to claim 15, comprising a hydrophilic polymer and a precursor substrate, the hydrophilic polymer being covalently bonded to a surface of the precursor substrate to the extent that a ratio of the hydrophilic polymer of the modified substrate that is not covalently bonded to the surface of the precursor substrate to the total of the hydrophilic polymer of the modified substrate is 15 weight percent or less and a number of adhered human blood platelets is 10/4.3x10³ μm² or less when the modified substrate is

PATENT APPLN. NO. 10/524,892
RESPONSE UNDER 37 C.F.R. §1.116

PATENT
FINAL

brought into contact with human blood which contains heparin with a concentration of 50 U/mL at 37°C for one hour, wherein the hydrophobic polymer substrate is a hydrophobic polymer comprising polymethylmethacrylate and an adsorptivity of the modified substrate to interleukin-6 is at least 0.1 ng/cm².

17. (previously presented) The modified substrate according to claim 1, wherein the precursor substrate is a medical substrate.

18. (canceled)

19. (withdrawn) A separation membrane comprising the modified substrate according to claim 1.

20. (withdrawn) The separation membrane according to claim 19, wherein the separation membrane is a hollow fiber membrane.

21. (withdrawn) The separation membrane according to claim 20, wherein the hydrophilic polymer is bonded on the inner surface of the hollow fiber membrane.

PATENT APPLN. NO. 10/524,892
RESPONSE UNDER 37 C.F.R. §1.116

PATENT
FINAL

22. (withdrawn) The separation membrane according to claim 21, wherein the hydrophilic polymer is further bonded on the inside of the hollow fiber membrane.

23. (withdrawn) A separation membrane of biogenic substances comprising the separation membrane according to claim 19.

24. (withdrawn) A system comprising a plurality of the modified substrates according to claim 1.

25. (withdrawn) The system according to claim 24, wherein the system comprising a plurality of the modified substrates composed of different materials.

26. (withdrawn) The system according to claim 24, wherein the system is a separation membrane system comprising a port element, a separation membrane, and a circuit, and at least a part of the port element, the separation membrane, and the circuit comprises the modified substrate.

27. (withdrawn - previously presented) A method for producing the modified substrate as set forth in claim 1, comprising a step

PATENT APPLN. NO. 10/524,892
RESPONSE UNDER 37 C.F.R. §1.116

PATENT
FINAL

of irradiating the substrate with radiation while the substrate is brought into contact with an aqueous solution containing a hydrophilic polymer and an antioxidant.

28. (withdrawn) The method for producing a modified substrate according to claim 27, wherein the substrate is immersed in the aqueous solution containing a hydrophilic polymer and an antioxidant in order to bring the substrate into contact with the aqueous solution.

29. (withdrawn) The method for producing a modified substrate according to claim 27, wherein the adsorptivity to cytokine of the modified substrate after irradiating with radiation is at least 90% of the adsorptivity to cytokine of the substrate before modification.

30. (withdrawn) The method for producing a modified substrate according to claim 29, wherein the cytokine is interleukin-6.

31. (withdrawn) The method for producing a modified substrate according to claim 29, wherein the substrate comprises a hydrophobic polymer.

PATENT APPLN. NO. 10/524,892
RESPONSE UNDER 37 C.F.R. §1.116

PATENT
FINAL

32. (withdrawn) The method for producing a modified substrate according to claim 27, wherein the substrate is a separation membrane.

33. (withdrawn) The method for producing a modified substrate according to claim 32, wherein the separation membrane is a hollow fiber membrane.

34. (withdrawn) The method for producing a modified substrate according to claim 33, wherein the inside of the hollow fiber membrane is filled with the aqueous solution containing a hydrophilic polymer and an antioxidant in order to bring the hollow fiber membrane into contact with the aqueous solution.

35. (withdrawn) The method for producing a modified substrate according to claim 34, wherein the outside of the hollow fiber membrane is further brought into contact with the aqueous solution.

36. (withdrawn) The method for producing a modified substrate according to claim 32, wherein the aqueous solution is filtered through the separation membrane in order to bring the separation membrane into contact with the aqueous solution.

PATENT APPLN. NO. 10/524,892
RESPONSE UNDER 37 C.F.R. §1.116

PATENT
FINAL

37. (withdrawn) A method for producing a system comprising a step of irradiating a plurality of substrates with radiation at the same time while the system comprising the plurality of substrates is brought into contact with an aqueous solution containing a hydrophilic polymer and an antioxidant.

38. (withdrawn) The method for producing a system according to claim 37, wherein the plurality of substrates are composed of different materials.

39. (withdrawn) The method for producing a system according to claim 37, wherein the system is a separation membrane system comprising a port element, a separation membrane, and a circuit, and the method comprises a step of irradiating the whole separation membrane system with radiation while the separation membrane system is brought into contact with the aqueous solution containing a hydrophilic polymer and an antioxidant.

40. (previously presented) The modified substrate according to claim 1, wherein the hydrophilic polymer is immobilized on the precursor substrate.